

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Inventors: Tateishi et al.  
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Title: Adhesive Patch

## Declaration by AMANO, Satoshi hereby declare:

1. I am a co-inventor of the above-referenced patent application and familiar with its teachings.

2. We performed experiments comparing the effects of three patch compositions containing different absorption promoters on skin permeation of bisoprolol. The ingredients of each patch composition are shown in Table 1. These patches were prepared using the procedures described in Examples 1 to 3 of the above-referenced patent application. Ingredients were identical except for the absorption promoter. Bisoprolol flux was examined according to the skin penetration tests described in Test 1 as paragraph [0049] of the above-referenced patent application. Results are shown in Table 2 and Figure 1.

3. The results show that using isopropyl myristate as the absorption promoter in combination with sodium acetate in Test example 1 resulted in significantly higher skin

permeation of bisoprolol compared to oleyl alcohol in combination with sodium acetate in Test example 2 or isostearyl alcohol in combination with sodium acetate in Test example 3.

I hereby declare that all statements herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or by imprisonment, or both, under §1001 of Title 18 of the United States code, and that such willful statements may jeopardize the validity of the application, any patent issuing there upon, or any patent to which this verified statement is directed.

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Date: 02/01/10

Table 1: Compositions of test examples

Test example	1	2	3
Bisoprolol fumarate	10.0%	10.0%	10.0%
Sodium acetate	4.5%	4.5%	4.5%
Isopropyl myristate	5.0%	-	-
Oleyl alcohol	-	5.0%	-
Isostearyl alcohol	-	-	5.0%
Liquid paraffin	15.0%	15.0%	15.0%
SIS block copolymer	8.0%	8.0%	8.0%
Acrylic adhesive*	18.5%	18.5%	18.5%
Allycyclic saturated hydrocarbon resin	39.0%	39.0%	39.0%

\*2-ethylhexyl acrylate/vinyl acetate/acrylic acid copolymer

Table 2: Skin penetration of bisoprolol

absorption promoter	Isopropyl myristate	Oleyl alcohol	Isostearyl alcohol
Mean Max. Flux	38.7	28.9	24.7
S.D.	2.6	2.8	4.2

Figure 1: Skin penetration of bisoprolol

